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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,750	02/08/2005	Dorothea Ledergerber	PD/4-32616A	2731

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
HAGOPIAN, CASEY SHEA	
ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,750	LEDERGERBER ET AL.	
	Examiner	Art Unit	
	Casey S. Hagopian	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-8/2005 7/18/2005 5/8/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of applicant's Information Disclosure Statements filed 2/8/2005, 7/18/2005 and 5/8/2008.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9 and 10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 provides for the use of a composition for the treatment of inflammatory and hyperproliferative skin diseases and of cutaneous manifestations of immunologically-mediated diseases. Claim 10 provides for the use of a carrier vehicle to enhance penetration of an ascomycin into human skin, nail or mucosa. Since the

claims do not set forth any steps involved in the methods/processes, it is unclear what methods/processes applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebert et al. (USPN 5,626,866) in view of Schopf ("Pimecrolimus (Novartis)" *IDrugs*. 1999 Nov;2(11):1197-200. Abstract Only).

Ebert teaches a transdermal or transmucosal drug delivery device comprising a drug in gelled form (abstract). Ebert defines "drug" to include immunosuppressives (col. 5, line 37). Said gelled drug can also include a penetration enhancer selected from a group consisting of a solvent, a cell-envelope disordering compound and mixtures thereof (claim 19). Ebert explains that the flux of a drug across the skin or mucosa can be altered by utilizing penetration enhancers which are comprised of two major categories, cell-envelope disordering compounds and solvents (col. 5, lines 49-52). Binary systems can also be utilized in which both cell-envelope disordering compounds and solvents are present (col. 5, lines 52-54). Preferred cell-envelope disordering compounds include isopropyl myristate (i.e., a "further solvent") and oleyl alcohol (i.e., a fatty alcohol) and preferred solvents include propanol (i.e., a C_3 alkanol) (col. 6, lines 12-14 and 20; claim 20). Ebert incorporates Cooper (USPN 4,537,776) by reference which discusses binary systems (see col. 6, lines 25-30 of Ebert) and teaches that the binary system is typically present in amounts of about 10% to 99.9%, preferably about 25% to about 99.9% of the entire composition (see col. 7, lines 29-37 of Cooper). Ebert also teaches including hydroxypropyl cellulose in the gelled drug composition in order to increase viscosity (col. 9, lines 64-67; claim 8).

Ebert is silent to the specific combination of isopropyl myristate (i.e., a "further solvent"), oleyl alcohol (i.e., a fatty alcohol) and propanol (i.e., a C_3 alkanol).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the aforementioned components with a reasonable expectation of success because the prior art suggests the generic combination of solvents and cell-envelope disordering compounds and lists a finite number of solvents and cell-envelope disordering compounds. Thus, one of ordinary skill in the art would have been able to envisage the particular combination of isopropyl myristate (i.e., a "further solvent"), oleyl alcohol (i.e., a fatty alcohol) and propanol (i.e., a C_3 alkanol). Also, each component is described as a permeation enhancer. Thus, it would have also been obvious to one of ordinary skill in the art to combine known ingredients known for the same purpose (see MPEP § 2144.06(I)).

Ebert is also silent to the 3-component solvent mixture being "at least 40% of the total weight of the composition".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the binary mixture taught by Ebert in amounts of at least 40% with a reasonable expectation of success because the prior art teaches generically binary systems in amounts of about 10% to 99.9%, preferably about 25% to about 99.9%. It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize composition by way of routine experimentation because "[W]here the general conditions of a claim are disclosed in the prior art, it is not

inventive to discover the optimum or workable ranges by routine experimentation" (see MPEP § 2144.05(II)).

Ebert is also silent to an ascomycin such as pimecrolimus for treatment of inflammatory and hyperproliferative skin diseases or cutaneous manifestations or immunologically-mediated diseases.

Schopf teaches that pimecrolimus is an ascomycin macrolactum derivative which inhibits T-cell and mast cell activation (abstract), i.e., exhibit immunosuppressive effects. Schopf also teaches that in 1998, topical and oral formulations were being utilized in clinical trials for the treatment of psoriasis and allergic dermatitis and in 1999, clinical trials began for the treatment of atopic dermatitis (abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include an ascomycin and in particular, pimecrolimus in the composition of Ebert for the treatment of inflammatory and hyperproliferative skin diseases or cutaneous manifestations or immunologically-mediated diseases with a reasonable expectation of success because Ebert teaches that immunosuppressives are suitable in the transdermal drug delivery device and Schopf suggests said pimecrolimus may be used in topical compositions to inhibit T-cell and mast cell activation for treatment of psoriasis, allergic dermatitis and atopic dermatitis.

It should be noted that claims 1-6 are product claims and any intended use recitation such as "for use in the treatment of inflammatory and hyperproliferative skin diseases and of cutaneous manifestations of immunologically-mediated diseases" in claim 7 does not alone show patentable distinction. A recitation of intended use of the

claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In other words, if the prior art structure is capable of performing the intended use, then it meets the claim. Claim 7 does not further limit the composition of claim 1, therefore the references read on claim 7 as well.

Thus, the combined teachings of Ebert and Schopf render the instant claims obvious.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebert et al. (USPN 5,626,866) in view of Ormerod et al. (WO 99/24036).

Ebert teaches a transdermal or transmucosal drug delivery device comprising a drug in gelled form (abstract). Ebert defines "drug" to include immunosuppressives (col. 5, line 37). Said gelled drug can also include a penetration enhancer selected from a group consisting of a solvent, a cell-envelope disordering compound and mixtures thereof (claim 19). Ebert explains that the flux of a drug across the skin or mucosa can be altered by utilizing penetration enhancers which are comprised of two major categories, cell-envelope disordering compounds and solvents (col. 5, lines 49-52). Binary systems can also be utilized in which both cell-envelope disordering compounds and solvents are present (col. 5, lines 52-54). Preferred cell-envelope disordering compounds include isopropyl myristate (i.e., a "further solvent") and oleyl alcohol (i.e., a fatty alcohol) and preferred solvents include propanol (i.e., a C_3 alkanol) (col. 6, lines 12-14 and 20; claim 20). Ebert incorporates Cooper (USPN 4,537,776) by reference

which discusses binary systems (see col. 6, lines 25-30 of Ebert) and teaches that the binary system is typically present in amounts of about 10% to 99.9%, preferably about 25% to about 99.9% of the entire composition (see col. 7, lines 29-37 of Cooper). Ebert also teaches including hydroxypropyl cellulose in the gelled drug composition in order to increase viscosity (col. 9, lines 64-67; claim 8).

Ebert is silent to the specific combination of isopropyl myristate (i.e., a "further solvent"), oleyl alcohol (i.e., a fatty alcohol) and propanol (i.e., a C_3 alkanol).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the aforementioned components with a reasonable expectation of success because the prior art suggests the generic combination of solvents and cell-envelope disordering compounds and lists a finite number of solvents and cell-envelope disordering compounds. Thus, one of ordinary skill in the art would have been able to envisage the particular combination of isopropyl myristate (i.e., a "further solvent"), oleyl alcohol (i.e., a fatty alcohol) and propanol (i.e., a C_3 alkanol). Also, each component is described as a permeation enhancer. Thus, it would have also been obvious to one of ordinary skill in the art to combine known ingredients known for the same purpose (see MPEP § 2144.06(I)).

Ebert is also silent to the 3-component solvent mixture being "at least 40% of the total weight of the composition".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include the binary mixture taught by Ebert in amounts of at least 40% with a reasonable expectation of success because the prior art teaches generically

binary systems in amounts of about 10% to 99.9%, preferably about 25% to about 99.9%. It would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize composition by way of routine experimentation because "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation" (see MPEP § 2144.05(II)).

Ebert is also silent to an ascomycin such as pimecrolimus for treatment of inflammatory and hyperproliferative skin diseases or cutaneous manifestations or immunologically-mediated diseases.

Ormerod teaches a topical formulation for the treatment of a dermatological condition (e.g., psoriasis) comprising an immunosuppressive macrolide including SDZ ASM 981 (i.e., pimecrolimus) and a permeation modulator (page 1, lines 1-7; claim 15). Ormerod also teaches that the permeation enhancer can be used in conjunction with a solvent system (i.e., a binary system) to optimize the passage of the drug across the stratum corneum (page 6, lines 1-10). Ormerod teaches that the immunosuppressive macrolide is present in amounts up to 10% and 0.05% to 2% is most preferable in the tretment of eczema (page 6, lines 12-22).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include pimecrolimus in the composition of Ebert for the treatment of inflammatory and hyperproliferative skin diseases or cutaneous manifestations or immunologically-mediated diseases with a reasonable expectation of success because Ebert teaches that immunosuppressives are suitable in the

transdermal drug delivery device and Ormerod suggests topical compositions comprising an immunosuppressive macrolide such as pimecrolimus, permeation enhancers and solvents may successfully be used to treat dermatological conditions such as psoriasis and eczema.

It should be noted that claims 1-6 are product claims and any intended use recitation such as "for use in the treatment of inflammatory and hyperproliferative skin diseases and of cutaneous manifestations of immunologically-mediated diseases" in claim 7 does not alone show patentable distinction. A recitation of intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. In other words, if the prior art structure is capable of performing the intended use, then it meets the claim. Claim 7 does not further limit the composition of claim 1, therefore the references read on claim 7 as well.

Thus, the combined teachings of Ebert and Ormerod render the instant claims obvious.

Conclusion

All claims have been rejected; no claims are allowed.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Casey Hagopian whose telephone number is 571-272-

6097. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Casey S Hagopian/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615